IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicant:	Virgil L. Woods, Jr.
Title:	METHODS FOR CRYSTALLOGRAPHIC STRUCTURE DETERMINATION EMPLOYING HYDROGEN EXCHANGE ANALYSIS
Appl. No.:	10/688,193
Filing Date:	10/27/2003
Examiner:	NOAKES, Suzanne Marie
Art Unit:	1656
Confirmation Number:	6673

COMMENTS ON STATEMENT OF REASONS FOR ALLOWANCE

Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450
Sir:

In response to the Examiner's Statement of Reasons for Allowance dated May 25, 2007, Applicant respectfully submits the following comments. This communication is timely filed along with the payment of the issue fee.

Revision of the Examiner's Statement of Reasons for Allowance is respectfully requested for clarification of the record. Clarifications requested by the Applicant are reflected in the marked up version of the Examiner's Statement of Reasons for Allowance reproduced below. Specifically, proposed deletions of text is indicated by strikethrough and proposed additions to the text is indicated by underline.

The science of protein crystallography is at best unpredictable and more of an art than a science. Many different factors contribute to the unpredictability and these are outlined, for example, in MacPherson, A. (Current Approaches to Macromolecular Crystallization, European Journal of Biochemistry, 1990, Vol. 189, pp. 1-23), who states there are 25 different parameters that influence the crystallization of any given protein, however, knowing which ones are the essential factors for any particular protein is never clear and can not be inferred. There are some techniques which are known that may increase the chance that protein will crystallize such as manipulating the N-terminus or C-terminus which ~~are~~ often times are not well ordered and at times can preclude crystallization of a protein. However, ~~what~~ **one of the features that** makes the instant methods novel over the prior art is the ability to determine exactly, down to single amino acids, which regions are unstructured. This gives an enormous advantage to the protein crystallographer to improve the chances that a protein might crystallize because it is well known that unstructured regions are not limited to only the C- or N-terminus and often times can be found anywhere in a protein. These unstructured regions are often times considered to be one of the largest obstacles to successful crystallization. ~~However, to date, other than~~ **In addition to** protein crystallography itself, or NMR methods, which are methods to determine the 3-D structures which would then give clues to where the unstructured regions exist, ~~there are no other methods~~ **the present invention provides a novel approach** to detail these unstructured regions. Herein lies the problem, however, when the protein a skilled artisan is working with does not crystallize and there is no analogous structure, how does one know where the unstructured regions exist, or if they exist at all? Although the method of hydrogen exchange analysis has been known for many years, the method has mainly been utilized in determining the steps involved in protein folding. The leap from **evaluating** protein folding to

achieving protein crystallization and improving the chances that a protein will crystallize or improving the quality of a protein that has already been crystallized by ~~**deleted**~~ **deleting** the unstructured regions is both novel and non-obvious. The allowed claims are 1-42.

Although no fee is believed to be associated with filing of this communication, the Commissioner is hereby authorized to charge any unpaid amount to Deposit Account No. 19-0741.

Respectfully submitted,

Date 8/17/07 By _____

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